

_		SECONOL DISTING	
	<110%	Wolfrain, Lawrence A Letterio, John J	
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tgg ctg cta Trp Leu Leu	gtg ctg Val Leu 20	acg cct Thr Pro	ggc cgg Gly Arg 25	ccg Pro	gcc Ala	gcc Ala	gga Gly	ctg Leu 30	tcc Ser	acc Thr	96
tgc aag acc Cys Lys Thr 35	atc gac Ile Asp	atg gag Met Glu	ctg gtg Leu Val 40	aag Lys	cgg Arg	aag Lys	cgc Arg 45	atc Ile	gag Glu	gcc Ala	144
att cgc ggc Ile Arg Gly 50	cag att Gln Ile	ctg tcc Leu Ser 55	aag ctt Lys Leu	cgg Arg	ctt Leu	gcc Ala 60	agc Ser	ccc Pro	ccg Pro	agc Ser	192
cag ggg gac Gln Gly Asp 65	gtg ccg Val Pro	ccc ggc Pro Gly 70	ccg ctg Pro Leu	cct Pro	gag Glu 75	gca Ala	gta Val	ctg Leu	gct Ala	ctt Leu 80	240
tac aac agt Tyr Asn Ser	acc cgc Thr Arg 85	gac cgg Asp Arg	gta gcc Val Ala	ggg Gly 90	gaa Glu	agt Ser	gtc Val	gaa Glu	ccg Pro 95	gag Glu	288
ccc gag cca Pro Glu Pro	gag gcg Glu Ala 100	gac tac Asp Tyr	tac gcc Tyr Ala 105	Lys	gag Glu	gtc Val	acc Thr	cgc Arg 110	gtg Val	cta Leu	336
atg gtg gaa Met Val Glu 115	Ser Gly	aac caa Asn Gln	atc tat Ile Tyr 120	gat Asp	aaa Lys	ttc Phe	aag Lys 125	ggc Gly	acc Thr	ccc Pro	384
cac agc tta His Ser Leu 130	tat atg Tyr Met	ctg ttc Leu Phe 135	Asn Thi	tcg Ser	gag Glu	ctc Leu 140	cgg Arg	gaa Glu	gcg Ala	gtg Val	432
ccg gaa cct Pro Glu Pro 145	gta ttg Val Leu	ctc tct Leu Ser 150	cgg gca Arg Ala	a gag a Glu	ctg Leu 155	cgc Arg	ctg Leu	ctg Leu	agg Arg	ctc Leu 160	480
aag tta aaa Lys Leu Lys	gtg gag Val Glu 165	Gln His	gtg gaq Val Gli	g cta 1 Leu 170	tac Tyr	cag Gln	aaa Lys	tac Tyr	agc Ser 175	aat Asn	528
gat tcc tgc Asp Ser Trp	cgc tac Arg Tyr 180	ctc ago Leu Ser	aac cgo Asn Aro 185	g Leu	ctg Leu	gcc Ala	ccc Pro	agt Ser 190	gac Asp	tca Ser	576
ccg gag tgc Pro Glu Trp 195	Leu Ser	ttt gat Phe Asp	gtc acc Val The 200	c gga c Gly	gtt Val	gtg Val	cgg Arg 205	cag Gln	tgg Trp	ctg Leu	624
acc cgc aga Thr Arg Arg 210	ı gag gct ı Glu Ala	ata gag a Ile Glu 215	Gly Phe	t cgc e Arg	ctc Leu	agt Ser 220	Ala	cac His	tct Ser	tcc Ser	672
tct gac ago	aaa gat	aac aca	ctc ca	c gtg	gaa	att	aac	ggg	ttc	aat	720

Cont



Ser Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn Gly Phe As 225 230 235 24	
tct ggc cgc cgg ggt gac ctg gcc acc att cac ggc atg aac cgg cc Ser'Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pr 245 250 255	768 70
ttc ctg ctc ctc atg gcc acc ccg ctg gag agg gcc cag cac ctg ca Phe Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu Hi 260 265 270	c 816 s
agc tcc cgg cac cgc cga gac tac aag gat gac gac gac aag gcc ct Ser Ser Arg His Arg Arg Asp Tyr Lys Asp Asp Asp Lys Ala Le 275 280 285	
gat acc aac tac tgc ttc agc tcc acg gag aag aac tgc tgc gtg cg Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys Asn Cys Cys Val Ar 290 295 300	
cag ctc tac att gac ttc cgg aag gac ctg ggc tgg aag tgg att ca Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp Ile Hi 305 310 315 32	S
gaa ccc aag ggc tac cat gcc aat ttc tgc ctg ggg ccc tgt ccc ta Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu Gly Pro Cys Pro Ty 325 330 335	
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ctg gag cca ctg ccc atc gtg tac tac gtg ggc cgc aag ccc aag gt Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly Arg Lys Pro Lys Va 370 375 380	
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Cut O'

Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser 180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu 195 200 205

Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala His Ser Ser 210 215 220

Ser Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn Gly Phe Asn 225 230 235 240

Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro  $245 \hspace{1.5cm} 250 \hspace{1.5cm} 255$ 





Phe Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His Ser Ser Arg His Arg Arg Asp Tyr Lys Asp Asp Asp Lys Ala Leu 280 Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys Asn Cys Cys Val Arg 295 300 Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp Ile His 315 310 Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr 330 325 Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn 345 340 Gln His Asn Pro Gly Ala Ser Ala Ala Pro Cys Cys Val Pro Gln Ala 360 355 Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly Arg Lys Pro Lys Val 380 370 Glu Gln Leu Ser Asn Met Ile Val Arg Ser Cys Lys Cys Ser 390 385 <210> 10 362 <211> <212> DNA Artificial Sequence <213> <220> <223> Fusion oligonucleotide <400> gactacaagg atgacgacga caaggccctg gataccaact actgcttcag ctccacggag aagaactgct gcgtgcggca gctctacatt gacttccgga aggacctggg ctggaagtgg

O'n

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attcatgaac ccaagggctc catgccaatt tctgcctggg gccctgtccc tacatctgga 180
gcctagacac tcagtacagc aaggtcctgg ctctgtacaa ccagcacaac ccgggcgcgt 240
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Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr

Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala 70

Ser Ala Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile 90

Val Tyr Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met

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tgg ctg cta gtg Trp Leu Leu Val 20							96
tgc aag acc atc Cys Lys Thr Ile 35	gac atg ga Asp Met Gl	g ctg gtg u Leu Val 40	aag cgg Lys Arg	aag cgc Lys Arg 45	atc gag Ile Glu	gcc Ala	144
att cgc ggc cag Ile Arg Gly Gln 50		r Lys Leu					192
cag ggg gac gtg Gln Gly Asp Val 65							240
tac aac agt acc Tyr Asn Ser Thr	cgc gac co Arg Asp Ai 85	g gta gcc g Val Ala	ggg gaa Gly Glu 90	agt gtc Ser Val	gaa ccg Glu Pro 95	gag Glu	288
ccc gag cca gag Pro Glu Pro Glu 100	Ala Asp Ty	c tac gcc r Tyr Ala 105	aag gag Lys Glu	gtc acc Val Thr	cgc gtg Arg Val 110		336
atg gtg gaa ago Met Val Glu Ser 115							384
cac agc tta tat His Ser Leu Tyr 130		e Asn Thr				, ,	432
ccg gaa cct gta Pro Glu Pro Val 145							480
aag tta aaa gtg Lys Leu Lys Val							528
gat too tgg cgc Asp Ser Trp Arg 180	Tyr Leu Se						576
ccg gag tgg ctg Pro Glu Trp Leu 195							624
acc cgc aga gag	gct ata ga	ıg ggt ttt	cgc ctc	agt gcc	cac tct	tcc	672



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tct Ser	ggc Gly	cgc Arg	cgg Arg	ggt Gly 245	gac Asp	ctg Leu	gcc Ala	acc Thr	att Ile 250	cac His	ggc Gly	atg Met	aac Asn	cgg Arg 255	ccc Pro	768
ttc Phe	ctg Leu	ctc Leu	ctc Leu 260	atg Met	gcc Ala	acc Thr	ccg Pro	ctg Leu 265	gag Glu	agg Arg	gcc Ala	cag Gln	cac His 270	ctg Leu	cac His	816
agc Ser	tcc Ser	cgg Arg 275	cac His	cgc Arg	cga Arg	gcc Ala	ctg Leu 280	gat Asp	acc Thr	aac Asn	tac Tyr	tgc Cys 285	ttc Phe	agc Ser	tcc Ser	864
acg Thr	gac Asp 290	tac Tyr	aag Lys	gat Asp	gac Asp	gac Asp 295	gac Asp	aag Lys	gag Glu	aag Lys	aac Asn 300	tgc Cys	tgc Cys	gtg Val	cgg Arg	912
cag Gln 305	ctc Leu	tac Tyr	att Ile	gac Asp	ttc Phe 310	cgg Arg	aag Lys	gac Asp	ctg Leu	ggc Gly 315	tgg Trp	aag Lys	tgg Trp	att Ile	cat His 320	960
gaa Glu	ccc Pro	aag Lys	ggc Gly	tac Tyr 325	cat His	gcc Ala	aat Asn	ttc Phe	tgc Cys 330	ctg Leu	ggg	ccc Pro	tgt Cys	ccc Pro 335	tac Tyr	1008
atc Ile	tgg Trp	agc Ser	cta Leu 340	gac Asp	act Thr	cag Gln	tac Tyr	agc Ser 345	aag Lys	gtc Val	ctg Leu	gct Ala	ctg Leu 350	tac Tyr	aac Asn	1056
cag Gln	cac His	aac Asn 355	ccg Pro	ggc Gly	gcg Ala	tcg Ser	gcg Ala 360	gcg Ala	ccg Pro	tgc Cys	tgc Cys	gtg Val 365	ccg Pro	cag Gln	gcg Ala	1104
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Maturation cleavage site



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Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala 35 40 45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser
50 55 60

Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu 65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val Glu Pro Glu 85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu 100 105 110

Met Val Glu Ser Gly Asn Gln Ile Tyr Asp Lys Phe Lys Gly Thr Pro  $115 \\ 120 \\ 125$ 

His Ser Leu Tyr Met Leu Phe Asn Thr Ser Glu Leu Arg Glu Ala Val 130  $\phantom{000}$  135  $\phantom{000}$  140

Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu Leu Arg Leu 145 150 155 160

Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn 165 170 175

Asp Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser 180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu 195 200 205

Thr Arg Arg Glu Ala Ile Glu Gly Phe Arg Leu Ser Ala His Ser Ser 210 215 220

Ser Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn Gly Phe Asn 225 230 235 240



Ser Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro 245 250 255

Phe Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu His 260 265 270

Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser 275 280 285

Thr Asp Tyr Lys Asp Asp Asp Asp Lys Glu Lys Asn Cys Cys Val Arg 290 295 300

Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp Ile His 305 310 315 320

Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr 325 330 335

Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn 340 345 350

Gln His Asn Pro Gly Ala Ser Ala Ala Pro Cys Cys Val Pro Gln Ala 355 360 365

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Glu Gln Leu Ser Asn Met Ile Val Arg Ser Cys Lys Cys Ser 385 390 395

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agcctagaca ctcagtacac aaggtcctgg ctctgtacaa ccagcacaac ccgggcgcgt 240
cggcggcgcc gtgctgcgtg ccgcaggcgc tggagccact gcccatcgtg tactacgtgg 300
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Arg Lys Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His 35 40 45

Ala Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr 50 60

Gln Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala 65 70 75 80

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	gact cetgetgett teteceteaa eeteaaatta tteaggacta teacetacet 24	0
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	ggtt cccgctctcc gaagtgccgt ggggcgccgc ctccccc atg ccg ccc 35  Met Pro Pro 1	6
	g ctg cgg cta ctg ccg ctt ctg ctc cca ctc ccg tgg ctt cta 40 y Leu Arg Leu Leu Pro Leu Leu Pro Leu Pro Trp Leu Leu 10 15	4
gtg ct	g acg ccc ggg agg cca gcc gcg gga ctc tcc acc tgc aag acc 45	2



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									agt Ser							548
									gtg Val							596
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									aaa Lys 125							740
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									ttg Leu							836
gtg Val	gag Glu 165	caa Gln	cat His	gtg Val	gaa Glu	ctc Leu 170	tac Tyr	cag Gln	aaa Lys	tat Tyr	agc Ser 175	aac Asn	aat Asn	tcc Ser	tgg Trp	884
cgt Arg 180	tac Tyr	ctt Leu	ggt Gly	aac Asn	cgg Arg 185	ctg Leu	ctg Leu	acc Thr	ccc Pro	act Thr 190	gat Asp	acg Thr	cct Pro	gag Glu	tgg Trp 195	932
ctg Leu	tct Ser	ttt Phe	gac Asp	gtc Val 200	act Thr	gga Gly	gtt Val	gta Val	cgg Arg 205	cag Gln	tgg Trp	ctg Leu	aac Asn	caa Gln 210	gga Gly	980
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aaa Lys	gat Asp	aac Asn 230	aaa Lys	ctc Leu	cac His	gtg Val	gaa Glu 235	atc Ile	aac Asn	ggg Gly	atc Ile	agc Ser 240	ccc Pro	aaa Lys	cgt Arg	1076
									atg Met							1124

260	265	270	275								
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atc cac gag ccc aag Ile His Glu Pro Lys 325											
ccc tat att tgg ago Pro Tyr Ile Trp Ser 340											
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Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser 50 55 60

Gln Gly Glu Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu 65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Ala Asp Pro Glu 85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu 100 105 110

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His Ser Ile Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg Glu Ala Val 130 135 . 140

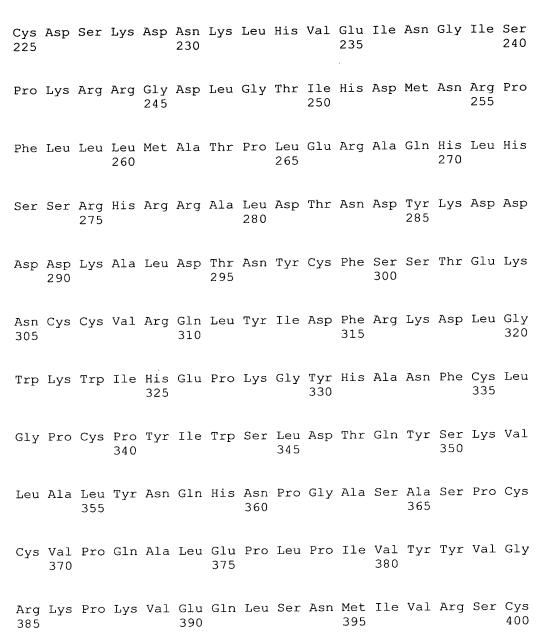
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Lys Ser Ser Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn 165 170 175

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Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu 195 200 205

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Cent.

Lys Cys Ser

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<220> <221> <222> <223>	misc_feature (1182)(1196) Encodes amino acid residues 1-5 of TGF-beta1	
<220> <221> <222> <223>	(1197)(1232)	
	<pre>misc_feature (1182)(1571) Encodes mature fusion protein</pre>	
<400>	20	

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gccgagggtt cccgctctcc gaagtgccgt ggggcgccgc ctccccc atg ccc ccc Met Pro Pro In Ser Gly Leu Arg Leu Leu Pro Leu Leu Leu Pro Leu Pro Trp Leu Leu Leu Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr Cys Lys Thr 20 30 356  atc gac atg gag ctg gtg aaa cgg aag cgc atc tcc acc tgc aag acc val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr Cys Lys Thr 20 30 35  atc gac atg gag ctg gtg aaa cgg aag cgc atc gaa gcc atc cgt gag gtl Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala Ile Arg Gly 40 45  cag atc ctg tcc aaa cta agg ctc gcc agt ccc caa agc cag ggg gag Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser Gln Gly Glu S5  gta ccc ccc ggc ccc ggc ccc gag ggg gtg ctc gct ttg tac aac agc Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu Tyr Asn Ser 70 80  acc cgc gac cgg gtg gca ggc gag agc gcc acc caa gag ccg gag ccc Glu Pro Pro Glu Pro 80 80  gaa gcg gac tac tat gct aaa gag gtc acc cac gag ccg gag ccc Glu Pro 80 80  gaa gcg gac tac tat gct aaa gag gtc acc cgc gtg ct Bro Glu Pro 90 80 80  gaa gcg gac tac tat gct aaa gag gtc acc cgc gtg ct atg gag cg gac Glu Pro 80 80  gaa gcg gac tac tat gct aaa gag gtc acc cgc gtg ct atg pro Glu Pro 80 80  gaa gcg gac tac tat gct aaa gag gtc acc cgc gtg ct atg gag cg gac Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu Met Val Asp 110  cgc aac aac gcc atc tat gag aaa acc aaa gac atc tca cac agt ata Arg Asn Asn Ala Ile Tyr Glu Lys Thr Lys Asp Ile Ser His Ser Ile 120  tat atg ttc ttc aat acg tca gac att cgg gaa gca gtg ccc gaa ccc Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg Glu Ala Val Pro Glu Pro 135  cca ttg ctg tcc cgt gca gag ctg cgc ttg cag aga tta aaa tca agt Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Glu Ala Val Pro Glu Pro 145  cca ttg ctg tcc cgt gca gag ctg ccc cac aga att tcc ttg cac acc act tac acc act tac acc act tac acc ac	caccgcgact cctg	ctgctt tctccctca	a cctcaaatta	ttcaggacta tca	cctacct 240
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Ser Gly Leu Arg Leu Leu Pro Leu Leu Pro Leu Pro Trp Leu Leu 15  gtg ctg acg ccc ggg agg cca gcc gcg gga ctc tcc acc tgc aag acc val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr Cys Lys Thr 20  atc gac atg gag ctg gtg aaa cgg aag cgc atc gaa gcc atc cgt ggc Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala Ile Arg Gly 40  cag atc ctg tcc aaa cta agg ctc gcc agt ccc cca agc cag ggg gag Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser Gln Gly Glu 65  gta ccg ccc ggc ccg ctg ccc gag gcg gtg ctc gct ttg tac aac agc Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu Tyr Asn Ser 70  acc cgc gac cgg gtg gca ggc gag agc gcc gac cca gag ccg gag ccc Glu Ala Asp Arg Val Ala Gly Glu Ser Ala Asp Pro Glu Pro Glu Pro Glu Pro 85  gaa gcg gac tac tat gct aaa ggc gcc acc cgc gtg ctc gcc gag ccg gag ccc Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu Met Val Asp 100  cgc aac aac gcc atc tat gag aaa acc aaa gac atc tca cac agt ata Arg Asn Asn Ala Ile Tyr Glu Lys Thr Lys Asp Ile Ser His Ser Ile 120  tat atg ttc ttc aat acg tca gac agc atc cgg gaa gca gtg gcc gac cac gtg ccc gaa ccc Tyr Met Phe Asn Thr Ser Asp Ile Arg Glu Ala Val Pro Glu Pro Glu Pro 140  cca ttg ctg tcc cgt gca gag ctc ctc acc aga aga tta aaa tca agt Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu Lys Ser Ser 150  gtg gag caa cat gtg gaa ctc tac cag aaa tat aac acc acc agt tac atg gtg gac cac ttg ctg tcc cgt gca gac ctc tac cac aga tta aaa tca agt Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu Lys Ser Ser Ire 150  gtg gag caa cat gtg gaa ctc tac cag aaa tat aac acc acc acc acc acc acc acc	gccgagggtt cccg	ctctcc gaagtgccg	t ggggcgccgc	Met Pr	-
Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr Cys Lys Thr 20  atc gac atg gag ctg gtg aaa cgg aag cgc atc gaa gcc atc ggg ggc Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala Ile Arg Gly 40  cag atc ctg tcc aaa cta agg ctc gcc agt ccc cca agc cag ggg gag Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser Gln Gly Glu 65  gta ccg ccc ggc ccg ctg ccc gag gcg gtg ctc gct ttg tac aac agc Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu Tyr Asn Ser 70  acc cgc gac cgg gtg gca ggc gag agc gcc gac cca gag ccg gag ccc 644  Thr Arg Asp Arg Val Ala Gly Glu Ser Ala Asp Pro Glu Pro Glu Pro 85  gaa gcg gac tac tat gct aaa gag gtc acc cgc gtg cta atg gtg gac Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu Met Val Asp 100  cgc aac aac gcc atc tat gag aaa acc aaa gac atc tca cac agt ata Arg Asn Asn Ala Ile Tyr Glu Lys Thr Lys Asp Ile Ser His Ser Ile 120  tat atg ttc ttc aat acg tca gac att cgg gaa gca gtg ccc gaa ccc Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg Glu Ala Val Pro Glu Pro Ila Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu Lys Ser Ser 150  gtg gag caa cac act gtg gaa ctc tac cag aaa tat aaa tca aagt Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu Lys Ser Ser 150  gtg gag caa cat gtg gaa ctc tac cag aaa tat agc aac aat tcc tcg 884  Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn Asn Ser Trp 165  cgt tac ctt ggt aac cgg ctg ctg acc ccc act gat acg cct gag tag Ccc gtac ctt gct gca gcd ctg ctg ccc act gat acc ccc gag gag Arg Tyr Leu Gly Asn Arg Leu Leu Thr Pro Thr Asp Thr Pro Glu Trp	Ser Gly Leu Arg	Leu Leu Pro Leu	ctg ctc cca Leu Leu Pro	Leu Pro Trp Le	t cta 404 u Leu
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Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser Gln Gly Glu  gta ccg ccc ggc ccg ctg ccc gag gcg gtg ctc gct ttg tac aac agc Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu Tyr Asn Ser 70 acc cgc gac cgg gtg gca ggc gag agc gcc gac cca gag ccg gag ccc Thr Arg Asp Arg Val Ala Gly Glu Ser Ala Asp Pro Glu Pro Glu Pro 85 gaa gcg gac tac tat gct aaa gag gtc acc cgc gtg cta atg gtg gac Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu Met Val Asp 100 105 110  cgc aac aac gcc atc tat gag aaa acc aaa gac atc tca cac agt ata Arg Asn Asn Ala Ile Tyr Glu Lys Thr Lys Asp Ile Ser His Ser Ile 120 125 130  tat atg ttc tca aat acg tca gac atc tag gac atc tag gac gac gac gcg gac ccc Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg Glu Ala Val Pro Glu Pro 135 140  cca ttg ctg tcc cgt gca gag ctg ctg ctg cag aga tta aaa tca agt Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu Lys Ser Ser 150  gtg gag caa cat gtg gaa ctc tac cag aaa tat agc aac aat tcc tgg Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn Asn Asn Ser Trp 165  cgt tac ctt ggt aac cgg ctg ctg acc ccc act gat acg ct gag tgg Arg Tyr Leu Gly Asn Arg Leu Leu Thr Pro Thr Asp Thr Pro Glu Trp	atc gac atg gag Ile Asp Met Glu	Leu Val Lys Arg	Lys Arg Ile	Glu Ala Ile Ar	2 2
Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu Tyr Asn Ser 70  acc cgc gac cgg gtg gca ggc gag agc gcc gac cca gag ccc gag ccc Glu Ala Asp Arg Val Ala Gly Glu Ser Ala Asp Pro Glu Pro Glu Pro 85  gaa gcg gac tac tat gct aaa gag gtc acc cgc gtg cta atg gtg gac Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu Met Val Asp 105  cgc aac aac gcc atc tat gag aaa acc aaa gac atc tca cac agt ata Arg Asn Asn Ala Ile Tyr Glu Lys Thr Lys Asp Ile Ser His Ser Ile 120  tat atg ttc ttc aat acg tca gac att cgg gaa gca gtg ccc gaa ccc Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg Glu Ala Val Pro Glu Pro 135  cca ttg ctg tcc cgt gca gag ctg ctg ctg cag aga tta aaa tca agt Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu Lys Ser Ser 150  gtg gag caa cat gtg gaa ctc tac cag aaa tat agc aac aat tcc tgg Ser Ser 160  gtg gag caa cat gtg gaa ctc tac cag aaa tat agc aac aat tcc tgg Ash Ser Trp 165  cgt tac ctt ggt aac cgg ctg ctg acc ccc act gat acg cct gag tgg Arg Tyr Leu Gly Asn Arg Leu Leu Thr Pro Thr Asp Thr Pro Glu Trp	Gln Ile Leu Ser	aaa cta agg ctc Lys Leu Arg Leu	Ala Ser Pro	Pro Ser Gln Gl	J J J
Thr Arg Asp Arg Val Ala Gly Glu Ser Ala Asp Pro Glu Pro Glu Pro 85  gaa gcg gac tac tat gct aaa gag gtc acc cgc gtg cta atg gtg gac Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu Met Val Asp 105  cgc aac aac gcc atc tat gag aaa acc aaa gac atc tca cac agt ata Arg Asn Asn Ala Ile Tyr Glu Lys Thr Lys Asp Ile Ser His Ser Ile 120  tat atg ttc ttc aat acg tca gac att cgg gaa gca gtg ccc gaa ccc Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg Glu Ala Val Pro Glu Pro 135  cca ttg ctg tcc cgt gca gag ctg cgc ttg cag aga tta aaa tca agt Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu Lys Ser Ser 150  gtg gag caa cat gtg gaa ctc tac cag aaa tat agc aac aat tcc tgg 884  Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn Asn Ser Trp 165  cgt tac ctt ggt aac cgg ctg ctg acc ccc act gat acg cct gag tgg Arg Tyr Leu Gly Asn Arg Leu Leu Thr Pro Thr Asp Thr Pro Glu Trp	Val Pro Pro Gly	Pro Leu Pro Glu	gcg gtg ctc Ala Val Leu	Ala Leu Tyr As	c agc 596 n Ser
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Arg Asn Asn Ala Ile Tyr Glu Lys Thr Lys Asp Ile Ser His Ser Ile 120 125 130  tat atg ttc ttc aat acg tca gac att cgg gaa gca gtg ccc gaa ccc Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg Glu Ala Val Pro Glu Pro 135 140 145  cca ttg ctg tcc cgt gca gag ctg cgc ttg cag aga tta aaa tca agt Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu Lys Ser Ser 150 155 160  gtg gag caa cat gtg gaa ctc tac cag aaa tat agc aac aat tcc tgg Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn Asn Ser Trp 165 170 175  cgt tac ctt ggt aac cgg ctg ctg acc ccc act gat acg cct gag tgg Arg Tyr Leu Gly Asn Arg Leu Leu Thr Pro Thr Asp Thr Pro Glu Trp	Glu Ala Asp Tyr	Tyr Ala Lys Glu	Val Thr Arg	gtg cta atg gt Val Leu Met Va	l Asp
Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg Glu Ala Val Pro Glu Pro 135  cca ttg ctg tcc cgt gca gag ctg cgc ttg cag aga tta aaa tca agt Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu Lys Ser Ser 150  gtg gag caa cat gtg gaa ctc tac cag aaa tat agc aac aat tcc tgg Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn Asn Ser Trp 165  cgt tac ctt ggt aac cgg ctg ctg acc ccc act gat acg cct gag tgg P32  Arg Tyr Leu Gly Asn Arg Leu Leu Thr Pro Thr Asp Thr Pro Glu Trp		Ile Tyr Glu Lys	Thr Lys Asp	Ile Ser His Se	r Ile
Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu Lys Ser Ser  150  gtg gag caa cat gtg gaa ctc tac cag aaa tat agc aac aat tcc tgg Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn Asn Ser Trp  165  170  175  cgt tac ctt ggt aac cgg ctg ctg acc ccc act gat acg cct gag tgg Arg Tyr Leu Gly Asn Arg Leu Leu Thr Pro Thr Asp Thr Pro Glu Trp	Tyr Met Phe Phe		Ile Arg Glu	Ala Val Pro Gl	
Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn Asn Ser Trp 165 170 175  cgt tac ctt ggt aac cgg ctg ctg acc ccc act gat acg cct gag tgg Arg Tyr Leu Gly Asn Arg Leu Leu Thr Pro Thr Asp Thr Pro Glu Trp	Pro Leu Leu Ser	Arg Ala Glu Leu	cgc ttg cag Arg Leu Gln	Arg Leu Lys Se	a agt 836 r Ser
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Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser
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Gln Gly Glu Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu 65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Ala Asp Pro Glu 85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu 100 105 110

Met Val Asp Arg Asn Asn Ala Ile Tyr Glu Lys Thr Lys Asp Ile Ser 115 120 125

His Ser Ile Tyr Met Phe Phe Asn Thr Ser Asp Ile Arg Glu Ala Val 130 135 140

Pro Glu Pro Pro Leu Leu Ser Arg Ala Glu Leu Arg Leu Gln Arg Leu

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Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Ser Tyr Pro Tyr Asp 275 280 285

Val Pro Asp Tyr Ala Ser Leu Ala Leu Asp Thr Asn Tyr Cys Phe Ser 290 295 300

Ser Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg 305 310 315 320

Lys Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala 325 330 335

Asn Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln 340 345 350

Tyr Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser 355 360 365

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aag ctc ac Lys Leu Th 50						o Asp				192
ccg gag gt Pro Glu Va 65	g att to al Ile Se	c atc tar r Ile Ty 70	aac a Asn S	gt acc Ser Thr	agg gad Arg Asp 75	c tta p Leu	ctg Leu	Gln	gag Glu 80	240
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ccc tcc ga Pro Ser Gl	u Asn Al									384
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Artificial Sequence

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Lys Ala Ser Arg Arg Ala Ala Ala Cys Glu Arg Glu Arg Ser Glu Gln 85 90 95													
Glu Tyr Tyr Ala Lys Glu Val Tyr Lys Ile Asp Met Pro Ser His Leu 100 105 110													
Pro Ser Glu Asn Ala Ile Pro Pro Thr Phe Tyr Arg Pro Tyr Phe Arg 115 120 125													
Ile Val Arg Phe Asp Val Ser Thr Met Glu Lys Asn Ala Ser Asn Leu 130 135 140													
Val Lys Ala Glu Phe Arg Val Phe Arg Leu Gln Asn Pro Lys Ala Arg 145 150 155 160													

Val Ala Glu Gln Arg Ile Glu Leu Tyr Gln Ile Leu Lys Ser Lys Asp 165 170 175



Leu Thr Ser Pro Thr Gln Arg Tyr Ile Asp Ser Lys Val Val Lys Thr 180 185 190

Arg Ala Glu Gly Glu Trp Leu Ser Phe Asp Val Thr Asp Ala Val Gln 195 200 205

Glu Trp Leu His His Lys Asp Arg Asn Leu Gly Phe Lys Ile Ser Leu 210 215 220

His Cys Pro Cys Cys Thr Phe Val Pro Ser Asn Asn Tyr Ile Ile Pro 225 230 235 235

Asn Lys Ser Glu Glu Leu Glu Ala Arg Phe Ala Gly Ile Asp Gly Thr 245 250 255

Ser Thr Tyr Ala Ser Gly Asp Gln Lys Thr Ile Lys Ser Thr Arg Lys 260 265 270

Lys Thr Ser Gly Lys Thr Pro His Leu Leu Met Leu Leu Pro Ser 275 280 285

Tyr Arg Leu Glu Ser Gln Gln Ser Ser Arg Arg Lys Lys Arg Ala Leu 290 295 300

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Tyr Cys Phe Arg Asn Val Gln Asp Asn Cys Cys Leu Arg Pro Leu Tyr 325 330 335

Ile Asp Phe Lys Arg Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys 340 345 350

Gly Tyr Asn Ala Asn Phe Cys Ala Gly Ala Cys Pro Tyr Leu Trp Ser 355 360 365

Ser Asp Thr Gln His Thr Lys Val Leu Ser Leu Tyr Asn Thr Ile Asn 370 380

Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Ser Gln Asp Leu Glu Pro 385 390 395 400

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					ttt Phe											433
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gcc Ala	aga Arg 160	gtg Val	gcc Ala	gag Glu	cag Gln	cgg Arg 165	att Ile	gaa Glu	ctg Leu	tat Tyr	cag Gln 170	atc Ile	ctt Leu	aaa Lys	tcc Ser	529
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Con

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tgg at Trp Il														1105
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Lys Ala Ser Arg Arg Ala Ala Ala Cys Glu Arg Glu Arg Ser Glu Gln 85 90 95

Glu Tyr Tyr Ala Lys Glu Val Tyr Lys Ile Asp Met Pro Ser His Leu 100 105 110

Pro Ser Glu Asn Ala Ile Pro Pro Thr Phe Tyr Arg Pro Tyr Phe Arg 115 120 125

Ile Val Arg Phe Asp Val Ser Thr Met Glu Lys Asn Ala Ser Asn Leu 130 135 140

Val Lys Ala Glu Phe Arg Val Phe Arg Leu Gln Asn Pro Lys Ala Arg 145 150 155 160

Val Ala Glu Gln Arg Ile Glu Leu Tyr Gln Ile Leu Lys Ser Lys Asp 165 170 175

Leu Thr Ser Pro Thr Gln Arg Tyr Ile Asp Ser Lys Val Val Lys Thr 180 185 190

Arg Ala Glu Gly Glu Trp Leu Ser Phe Asp Val Thr Asp Ala Val Gln 195 200 205

Glu Trp Leu His His Lys Asp Arg Asn Leu Gly Phe Lys Ile Ser Leu 210 215 220

His Cys Pro Cys Cys Thr Phe Val Pro Ser Asn Asn Tyr Ile Ile Pro 225 230 235 240

Asn Lys Ser Glu Glu Leu Glu Ala Arg Phe Ala Gly Ile Asp Gly Thr 245 250 255



Ser Thr Tyr Ala Ser Gly Asp Gln Lys Thr Ile Lys Ser Thr Arg Lys 260 265 270

Lys Thr Ser Gly Lys Thr Pro His Leu Leu Leu Met Leu Leu Pro Ser 275 280 285

Tyr Arg Leu Glu Ser Gln Gln Ser Ser Arg Arg Lys Lys Arg Ala Leu 290 295 300

Asp Ala Ala Ser Tyr Pro Tyr Asp Val Pro Asp Tyr Ala Ser Leu Ala 305 310 315 320

Leu Asp Ala Ala Tyr Cys Phe Arg Asn Val Gln Asp Asn Cys Cys Leu 325 330 335

Arg Pro Leu Tyr Ile Asp Phe Lys Arg Asp Leu Gly Trp Lys Trp Ile 340 345 350

His Glu Pro Lys Gly Tyr Asn Ala Asn Phe Cys Ala Gly Ala Cys Pro 355 360 365

Tyr Leu Trp Ser Ser Asp Thr Gln His Thr Lys Val Leu Ser Leu Tyr 370 375 380

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48

a' cont

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Leu Arg Leu Thr Ser Pro Pro Glu Pro Ser Val Met Thr His Val Pro 50 55

Tyr Gln Val Leu Ala Leu Tyr Asn Ser Thr Arg Glu Leu Leu Glu Glu 75 65

Met His Gly Glu Arg Glu Glu Gly Cys Thr Gln Glu Thr Ser Glu Ser 90 85

Glu Tyr Tyr Ala Lys Glu Ile His Lys Phe Asp Met Ile Gln Gly Leu 105 110 100

Ala Glu His Asn Glu Leu Ala Val Cys Pro Lys Gly Ile Thr Ser Lys 120 115



Val Phe Arg Phe Asn Val Ser Ser Val Glu Lys Asn Gly Thr Asn Leu 130 135 140

Phe Arg Ala Glu Phe Arg Val Leu Arg Val Pro Asn Pro Ser Ser Lys 145 150 155 160

Arg Thr Glu Gln Arg Ile Glu Leu Phe Gln Ile Leu Arg Pro Asp Glu 165 170 175

His Ile Ala Lys Gln Arg Tyr Ile Gly Gly Lys Asn Leu Pro Thr Arg 180 185 190

Gly Thr Ala Glu Trp Leu Ser Phe Asp Val Thr Asp Thr Val Arg Glu
195 200 205

Trp Leu Leu Arg Arg Glu Ser Asn Leu Gly Leu Glu Ile Ser Ile His 210 215 220

Cys Pro Cys His Thr Phe Gln Pro Asn Gly Asp Ile Leu Glu Asn Val 225 230 235 240

His Glu Val Met Glu Ile Lys Phe Lys Gly Val Asp Asn Glu Asp Asp 245 250 255

His Gly Arg Gly Asp Leu Gly Arg Leu Lys Lys Gln Lys Asp His His 260 265 270

Asn Pro His Leu Ile Leu Met Met Ile Pro Pro His Arg Leu Asp Ser 275 280 285

Pro Gly Gln Gly Ser Gln Arg Lys Lys Arg Ala Leu Asp Thr Asn Asp 290 295 300

Tyr Lys Asp Asp Asp Asp Lys Ala Leu Asp Thr Asn Tyr Cys Phe Arg 305 310 315 320

Asn Leu Glu Glu Asn Cys Cys Val Arg Pro Leu Tyr Ile Asp Phe Arg 325 330 335

Gln Asp Leu Gly Trp Lys Trp Val His Glu Pro Lys Gly Tyr Tyr Ala 340 345 350

Asn Phe Cys Ser Gly Pro Cys Pro Tyr Leu Arg Ser Ala Asp Thr Thr 355 360 365

His Ser Thr Val Leu Gly Leu Tyr Asn Thr Leu Asn Pro Glu Ala Ser



380

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144

Ile Lys Lys Arg Val Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys

35

40

45

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Glu Tyr Tyr Ala Lys Glu Ile His Lys Phe Asp Met Ile Gln Gly Leu

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Val Phe Arg Phe Asn Val Ser Ser Val Glu Lys Asn Gly Thr Asn Leu 130 135

Phe Arg Ala Glu Phe Arg Val Leu Arg Val Pro Asn Pro Ser Ser Lys 145 155

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His Glu Val Met Glu Ile Lys Phe Lys Gly Val Asp Asn Glu Asp Asp 250



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Asn Pro His Leu Ile Leu Met Met Ile Pro Pro His Arg Leu Asp Ser 275 280 285

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Ile Asp Phe Arg Gln Asp Leu Gly Trp Lys Trp Val His Glu Pro Lys 340 345 350

Gly Tyr Tyr Ala Asn Phe Cys Ser Gly Pro Cys Pro Tyr Leu Arg Ser 355 360 365

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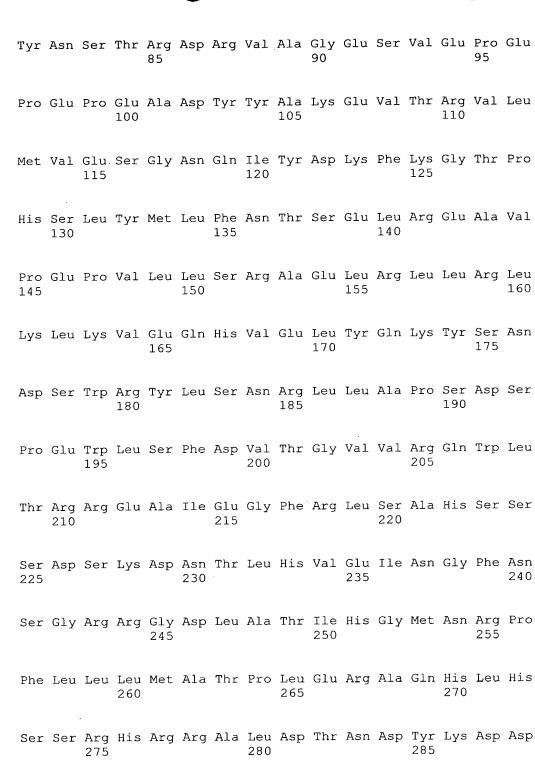
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al conti





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a'

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Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly

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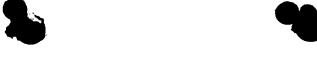
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Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser Ala Ala Pro Cys 



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Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu 65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Val Glu Pro Glu 85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu 100 105 110

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Ser Asp Ser Lys Asp Asn Thr Leu His Val Glu Ile Asn Gly Phe Asn 225 230 235 240

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Pro Pro Ser Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val
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Gln Gly Asp Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu 65 70 75 80

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